REMARKS

Claims 86, 91, 93, 95, 98-100, 108, 113, 115, 117, 120-122, 133 and 134 are currently pending. Claims 108, 113, 115, 117, 120-122 and 134 have been cancelled. Claims 91, 93, 95, 98-100 have been amended to remove multiple dependencies. Claims 135-140 have been added. Therefore, claims 86, 91, 93, 95, 98-100, 133, and 135-140 will be pending upon entry of the present amendment.

Support for new claims 135-137, can be found, for example, at least at page 3, line 36-38, of the specification as originally filed. Support for new claim 138 can be found, for example, at least at page 36, line 35. Support for new claim 139 can be found, for example, at least at page 8, lines 13-20. Support for new claim 140 can be found, for example, at least at page 3, line 28. No new matter has been added.

Cancellation of and/or amendments to the claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The cancellation of and/or amendments made to the claims are not related to any issues of patentability.

Applicants note with appreciation that the Examiner has withdrawn the rejection of claims 86, 91, 93-95, 96, 98-100, 108, 113, 115-117, 120-122 and 133-134 under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 86, 93, 95, 98, 100, 108, 115, 117, 120, 122, 133 and 134 under 35 U.S.C. §102(e)

Claims 86, 91, 93-95, 98, 100, 108, 113, 115-117, 120-122, 133 and 134 are rejected under 35 U.S.C. §102(e) as being anticipated by Blass *et al.* (U.S. Patent No. 6,537,969). Specifically, the Examiner asserts that Blass *et al.* discloses "the method for treating diseases of the nervous system including Parkinson's disease, Huntington's disease using the same pharmaceutical composition of the instant claims" and "the same pharmaceutical composition combining creatine and a neuroprotective agent as the instant claims."

Applicants disagree. Claims 108, 113, 115, 117, 120-122 and 134 have been cancelled, thus rendering the rejection of these claims moot. Applicants' claims 86, 91, 93-95, 98, 100, and 133 are entitled, under 35 U.S.C. 119(e), to the benefit of the filing date of U.S.S.N. 60/080,459, filed April 2, 1998. The effective 102 (e) date of Blass for the subject matter cited by the Examiner (i.e., the

pharmaceutical composition combing creatine, neuroprotective agent, antioxidants, riboflavin, and L-carnitine at column 5, lines 33-50) is September 1, 1998, which is subsequent to Applicants' priority date. Applicants note that the subject matter relied on by the Examiner in Blass's disclosure is not present in Blass's priority document (U.S.S.N. 60/063,165, filed October 24, 1997) and, therefore, is not entitled to the benefit of this 102 (e) date and thus is not prior art.

Accordingly, Applicants respectfully request that this rejection of claims 86, 91, 93-95, 98, 100, and 133 under 35 U.S.C. § 102 (e), be reconsidered and withdrawn.

Rejection of Claim 99 under 35 U.S.C. 103(a)

Claim 99 is rejected under 35 U.S.C. §103(a) as being unpatentable over Blass *et al.* (U.S. Patent No. 6,537,969). Specifically, the Examiner asserts that Blass *et al.* "generically disclosed pharmaceutical composition combining of creatine and a neuroprotective agent...and that the difference between the instant claims and the prior art is that the prior art has 2 active ingredients combining creatine and a neuroprotective agent whereas the instant claimed compositions has one additional neuroprotective agent or creatine compound." Applicants respectfully traverse.

Applicants' claim 99 is entitled, under 35 U.S.C. 119 (e), to the benefit of the filing date of U.S.S.N. 60/080,459, filed April 2, 1998. As described above, the effective 102 (e) date of Blass for the subject matter cited by the Examiner (i.e., the pharmaceutical composition combing creatine, neuroprotective agent, antioxidants, riboflavin, and L-carnitine at column 5, lines 33-50) is September 1, 1998, which is subsequent to Applicants' priority date. Applicants note that the subject matter relied on by the Examiner in Blass's disclosure is not present in Blass's priority document (U.S.S.N. 60/063,165, filed October 24, 1997) and, therefore, is not entitled to the benefit of this 102 (e) date and thus is not prior art.

Accordingly, Applicants respectfully request that this rejection of claim 99 under 35 U.S.C. § 103 (a), be reconsidered and withdrawn.

Rejection of Claims 86, 91, 93-95, 98-100 and 133 under 35 U.S.C. §112, first paragraph

Claims 86, 91, 93-95, 98-100 and 133 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner asserts that "Example 2 is a prophetic example, [A]pplicant has mouse models of Parkinson's disease such as MPTP. However, [A]pplicant has not guidance or examples for treating Parkinson's disease using pharmaceutical composition of a combination of creatine, creatine phosphate or a creatine

compound and a neuroprotective agent. Nor does [A]pplicants have any examples of MPTP model of the instant compounds working on the MPTP model."

Applicants respectfully disagree. First, Applicants note that working examples are not required. For example, the MPEP § 2164.02 states that "the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)." Applicants respectfully submit that the amount of disclosure in the application clearly would have enabled one of ordinary skill in the art to perform the methods of the invention without undue experimentation at the time the application was filed, as described in further detail below.

Applicants also note that the disclosure of invention set forth by Applicants in their application must be given the presumption of correctness and operativeness by the PTO, and the only relevant concern of the PTO under the circumstances should concern the truth of the assertions contained in the application. *In re Marzocchi*, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 1967); see also, *In re Bowen*, 492 F.2d 859, 181 U.S.P.Q. 48 (C.C.P.A. 1974). Applicants submit that the Office Action proffers nothing to controvert the truth of Applicants' assertions in the instant application. There are no references cited in the Office Action that controverts the truth of Applicants' assertion in the application, *e.g.*, combinations of creatine, creatine phosphate or a creatine compound and a neuroprotective agent are useful to treat Parkinson's disease.

Methods of using pharmaceutical compositions comprising creatine, creatine phosphate, or a creatine compound and a neuroprotective agent to treat Parkinson's are described throughout the instant specification. For example, the methods of using the combinations of the invention to treat nervous system diseases are described, for example, at least at page 3, lines 22-28, page 8, lines 22-25, and page 74, lines 9-14. Furthermore, other examples in the application (e.g., Example 4 on page 57) show the use of creatine in combination with other neuroprotective agents (e.g., nicotinamide). One of ordinary skill in the art at the time the application was filed would have been able to use the methods described in the specification to make and use the invention, e.g., combinations of creatine, creatine phosphate or a creatine compound and a neuroprotective agent to treat Parkinson's disease, without undue experimentation.

Furthermore, the effectivity of creatine on the MPTP mouse model of Parkinson's disease is accepted by the scientific community as evidence of the effectivity of creatine as a potential treatment of Parkinson's disease. The data from an experiment using creatine on a MPTP mouse model is cited on National Institute of Health's website for the clinical trials of creatine for the

treatment of Parkinson's (http://www.ninds.nih.gov/funding/research/parkinsonsweb /drug_summaries/ creatine.htm). This shows that one of ordinary skill in the art would have considered that the MPTP model does provide evidence that the compounds of the invention are useful for the treatment of Parkinson's disease. Furthermore, in the attached declaration of Belinda Tsao Nivaggioli, Ph.D., additional data for the use of creatine to treat Parkinson's disease are also presented.

Finally, Applicants' claims are directed to methods of treating Parkinson's disease by administrering an effective amount of combinations of creatine, creatine phosphate or a creatine compound and a neuroprotective agent, ***such that Parkinson's disease is treated.*** Therefore, Applicants' claimed invention is only directed to methods wherein Parkinson's disease is treated by the compounds of the invention, and ***not*** to methods wherein Parkinson's disease is not treated. The claims, as written, exclude methods of treatment which are not effective to treat Parkinson's disease, because all the steps of the claimed methods are not met.

Therefore, Applicants respectfully request that this rejection of the claims 86, 91, 93-95, 98-100 and 133 under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejection of Claims 108, 113, 115-117, 120-122 and 134 under 35 U.S.C. §112, first paragraph

Claims 108, 113, 115-117, 120-122 and 134 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully disagree. However, in the interest of expediting prosecution of the application, claims 108, 113, 115-117, 120-122, and 134 have been cancelled, thus rendering the rejection of these claims moot.

SUMMARY

It is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conference with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By _____

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